Internship Proposition
(one page max)

Master 2 GP Immunology & ImmunoIntervention (I^3)
2025-2026

Lab: CRCI2NA, UMR1307

Team: Team 12

Name and position of the supervisor:
- **GRAIN Audrey MD PhD pediatric oncology and hematology**
- **CLEMENCEAU Béatrice PhD immunologist**

Email of the supervisors: Beatrice.clémenceau@inserm.fr; Audrey.grain@chu-nantes.fr

Candidate (if internship filled): Mr Philippe Gardeton

Title of the internship: Identification of combination of antigens of interest comprising the CD24, in pediatric B-cell precursor lymphoblastic leukemia

Summary of the internship proposal:

Relapse or refractory B-cell precursors acute lymphoblalstic leukemia (BCP-ALL) are associated with a very poor prognosis in children. The emerging targeted therapy notably the anti-CD19 CAR-T cells (T-cells modified to express a chimeric antigen receptor (CAR) directed against the CD19), yielded early good results with 80% of patients in response. However, almost a half of the patients relapse during the first year post-CAR-T. The loss of the previously targeted antigen explains 40% of these high risk relapse.

A multi-antigen targeting strategy could avoid tumoral escape through antigen modulation, new targets are therefore needed, and efficient combination should be defined.

Previous research in the team allow to identify 13 antigen of interest highly expressed in primary BCP-ALL from pediatric patients. Then some cytotoxic assays were conducted, with monoclonal antibodies and T-cells genetically modified to express the murin CD16 and able of antibodies-dependant cellular cytotoxicity (ADCC) when used in combination with murin antobodies. Among these antigens, the antigen CD24 appear to be a targeted of interest by leading to highly effective ADCC-mediated lysis of BCP-ALL. However, as also described in other research group invoved in the ADCC strategy, no synergistic or additive effect was described, by using 2 or 3 antibodies in combination. Moreover, when 2 antibodies were added to the anti-CD24 antibody, a reduction of the ADCC activity was observed.

One hypothesis is that, the ADCC activity, which is dependent of the epitope on the antigen, and the accessibility of the Fc fragment, and may be improved by the use of polyclonal antibodies.

A second hypothesis is that the use of different modalities of recognition (for example CAR and ADCC) may improve the lysis observed.

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Research proposal:

During the intership, the candidate will explore the hypothesis previously described.

He will perform different cytotoxicity assays to compare the ADCC activity of different anti-CD24 murin antibodies, from different clones, recognizing different epitopes. He will then try to define efficient combinations of antibodies comprising a CD24 recognition.

Secondly, in order to compare different modalities of recognition, cytotoxicity assays using T-cell modified to express an anti-CD24 chimeric antigen receptor (CAR) will be envisaged.

Option(s) linked to the project:

☐ Clinical Research Profile (Recherche Clinique)
☐ Data Analyst Profile (Recherche et Analyse de Données Omiques)
☐ Experimental Biology Profile (Recherche Expérimentale)

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